REMARKS

In view of the above amendments and following remarks, applicants respectfully request reconsideration of the outstanding office action.

Pursuant to 37 CFR § 1.21, attached as an appendix is a version which contains markings to show changes made to the specification and the claims.

Enclosed herewith is a newly executed Combined Declaration and Power of Attorney form which correctly recites the chain of priority claimed for the present continuation-in-part application. In particular, the parent application pending at the time of filing the present application was not U.S. Patent Application Serial No. 09/057,416, filed April 8, 1998 (now abandoned), but instead U.S. Patent Application Serial No. 09/642,218 filed August 18, 2000. The recitation of the correct provisional patent application (Serial No. 60/043,202) has also been made. In addition to correcting the recitation of priority documents listed on the enclosed Combined Declaration and Power of Attorney forms, applicants have amended the specification to recite the proper chain of priority. Therefore, the objection to the previously submitted Combined Declaration and Power of Attorney forms has been overcome and should be withdrawn. Accompanying this Amendment is a Request for Corrected Filing Receipt.

In view of the above amendments canceling claims directed to non-elected subject matter (without prejudice), applicants also submit herewith a Request to Correct Inventorship Under 37 CFR § 1.48(b).

Applicants respectfully request that the objection to the drawings be held in abeyance until this case has been allowed.

The objection to the specification for failure to comply with the requirements of 37 C.F.R. § 1.821 *et seq.* has been overcome by the above amendment to the specification (specifically the description of Figures 15A-B). Therefore, this objection should be withdrawn.

The objection to claim 8 as being dependent on a rejected base claim has been rendered moot in view of the above amendments. Applicants request withdrawal of the objection.

The rejection of claim 9 under 35 U.S.C. § 112 (second paragraph) for indefiniteness is respectfully traversed in view of the above amendments.

The rejection of claims 1-3, 7, 9, and 49-56 under 35 U.S.C. § 112 (first paragraph) as lacking written descriptive support is respectfully traversed.

The U.S. Patent & Trademark Office ("PTO") has asserted that the invention as claimed encompasses any nucleic acid from a thermophilic organism that encodes any polymerase III enzyme subunit (page 8 of outstanding office action). Applicants respectfully disagree.

Applicants submit that the invention as presently claimed overcomes the above-identified basis of rejection, because the isolated nucleic acid as claimed is limited to those nucleic acids "from a *Thermus* species encoding a delta subunit of a DNA polymerase III-type enzyme" that are characterized by any one of the three structural features recited: either possessing "the nucleotide sequence of SEQ ID NO: 157," encoding "the amino acid sequence of SEQ ID NO: 158," or hybridizing to "the complement of SEQ ID NO: 157 under hybridization conditions comprising about 0.9M or less sodium citrate buffer at a temperature of at least about 37°C."

The PTO has acknowledged that the present application provides written descriptive support for the isolated DNA molecule of SEQ ID NO: 157 and isolated DNA molecules encoding the amino acid sequence of SEQ ID NO: 158 given that claims 8 and 9 as originally filed were only objected to as being dependent upon a rejection base claim. Therefore, the only issue is whether the present application provides sufficient written descriptive support for the limitations concerning an isolated DNA molecule that hybridizes to "the complement of SEQ ID NO: 157 under hybridization conditions comprising about 0.9M or less sodium citrate buffer at a temperature of at least about 37°C." Applicants submit that written descriptive support exists.

Applicants have identified the nucleotide sequence of SEQ ID NO: 157 and, thus, have inherently identified the complement thereof, which is what a DNA molecule homologous to SEQ ID NO: 157 would hybridize to under appropriate conditions (see page 30 at lines 7-21). The hybridization conditions specified in the various claims find descriptive support as follows: claims 1 and 71 (page 30, lines 13-15), claim 72 (page 30, lines 15-17), and claim 73 (page 35, lines 19-21; page 49, lines 9-27). Because the present application fully supports the conditions under which hybridization will occur and the

substrate to which hybridizing DNA molecules will be exposed, applicants submit that written descriptive support for the presently claimed genus exists.

Moreover, the present application also describes an assay to determine whether the protein encoded by a particular isolated nucleic acid is a delta subunit. This can be assessed by determining whether the encoded protein is capable of forming a clamp loader complex (along with a delta prime subunit and either a gamma or a tau subunit). Example 24 (page 107) specifies one such procedure, whereby the protein subunits are combined and a MonoQ column equilibrated in buffer A is used to determine whether the subunits form a clamp loader complex, which is distinguished by its (later) elution from the MonoQ column as compared to the individual subunits.

Because the present application fully describes the invention as presently claimed, applicants submit that the rejection of claims 1-3, 7, 9, and 49-56 under 35 U.S.C. § 112 (first paragraph) as lacking written descriptive support is improper and should be withdrawn.

The rejection of claims 1-3, 7, 9, and 49-56 under 35 U.S.C. § 112 (first paragraph) for lack of enablement is respectfully traversed.

The PTO has acknowledged that the present application enables the isolated DNA molecule of SEQ ID NO: 157 and isolated DNA molecules encoding the amino acid sequence of SEQ ID NO: 158 given that claims 8 and 9 as originally filed were only objected to as being dependent upon a rejection base claim. Therefore, the only issue is whether the present application fully enables the limitations concerning an isolated DNA molecule that hybridizes to "the complement of SEQ ID NO: 157 under hybridization conditions comprising about 0.9M or less sodium citrate buffer at a temperature of at least about 37°C." Applicants submit that one of ordinary skill in the art is fully able to practice the invention as claimed.

As noted above, applicants have identified the nucleotide sequence of SEQ ID NO: 157 and, thus, its complement. The hybridization conditions specified in the various claims are provided in the present application, also as noted above. By way of example, the present application also identifies a particular hybridization protocol at page 49, lines 9-27, indicating all of the steps that one of ordinary skill in the art would need to perform to obtain an isolated DNA molecule as presently claimed.

As noted above, Example 24 (page 107) identifies a procedure used to determine whether a particular isolated nucleic acid encodes a delta subunit, by determining

whether the encoded protein is capable of forming a clamp loader complex (along with a delta prime subunit and either a gamma or a tau subunit).

Because one of ordinary skill in the art is fully capable of performing a hybridization procedure as presently claimed, the presently claimed invention specifies structural limitations and the conditions for such hybridization, and one of ordinary skill in the art is fully capable of determining whether an encoded protein is able to form a clamp loader complex with cooperating enzyme subunits, applicants submit that the basis for the enablement rejection has been overcome.

For these reasons, the rejection of claims 1-3, 7, 9, and 49-56 for lack of enablement is improper and should be withdrawn.

In view of all of the foregoing, applicants respectfully submit that this application is in condition for allowance and such allowance is therefore requested.

Respectfully submitted,

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Date 3/18/03 Jane C. Wirszyla

APPENDIX
Version With Markings to Show Changes Made
Page 1 of 3

In reference to the amendments made herein, additions appear as underlined text while deletions appear as strikeout text, as indicated below.

In the Specification:

At page 1, lines 4-8:

The present application is a continuation-in-part of U.S. Patent Application Serial No. 09/642,218, filed August 18, 2000, as a continuation of U.S. Patent Application Serial No. 09/057,416, filed April 8, 1998, which claims the benefit of ~~U.S. Patent Application Serial No. 08/823,407 filed April 8, 1997, and~~ U.S. Provisional Patent Application Serial No. ~~60/143,202~~ 60/043,202 filed April 8, 1997, all of which are hereby incorporated by reference.

At page 17, lines 8-16:

FIGURES 15A-B show the alignments of the peptides obtained from *T.th.* α subunit, TTH1 (shown in A) and TTH2 (shown in B) with the amino acid sequences of the α subunits of other organisms. The amino acid number of these regions within each respective protein sequence are shown to the right. The abbreviations of the organisms are as follows. *E.coli* - *Escherichia coli* (SEQ ID NOS: 72 and 79 in 15A-B, respectively), *V.chol.*- *Vibrio cholerae* (SEQ ID NOS: 73 and 80 in 15A-B, respectively), *H.inf.* - *Haemophilus influenzae* (SEQ ID NOS: 74 and 81 in 15A-B, respectively), *R.prow.* - *Rickettsia prowazekii* (SEQ ID NOS: 75 and 82 in 15A-B, respectively), *H.pyl.* - *Helicobacter pylori* (SEQ ID NOS: 76 and 83 in 15A-B, respectively), *S.sp.* - *Synechocystis sp.* (SEQ ID NOS: 77 and 84 in 15A-B, respectively), *M.tub.* - *Mycobacterium tuberculosis* (SEQ ID NOS: 78 and 85 in 15A-B, respectively), *T.th.* - *Thermus thermophilus* (SEQ ID NOS: 61 and 60 in 15A-B, respectively).

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In the Claims:

1. (Amended) An isolated DNA molecule from a *Thermus* species ~~thermophilic bacterium, the isolated DNA molecule~~ encoding a delta subunit of a DNA polymerase III-type enzyme ~~subunit~~, the isolated DNA molecule either:

(i) comprising the nucleotide sequence of SEQ ID NO: 157;

(ii) encoding the amino acid sequence of SEQ ID NO: 158; or

(iii) hybridizing to the complement of SEQ ID NO: 157 under hybridization conditions comprising about 0.9M or less sodium citrate buffer at a temperature of at least about 37°C.

7. (Amended) The isolated DNA molecule according to claim ~~3~~ 1, wherein the *Thermus* species ~~thermophilic bacterium~~ is *Thermus thermophilus*.

8. (Amended) The isolated DNA molecule according to claim ~~7~~ 1, wherein the DNA molecule encodes the ~~delta subunit comprises an~~ amino acid sequence of ~~SEQ. ID. No.~~ SEQ ID NO:158.

9. (Amended) The isolated DNA molecule according to claim ~~7~~ 1, wherein the DNA molecule comprises ~~a~~ the nucleotide sequence of ~~SEQ. ID. No.~~ SEQ ID NO: 157 ~~or hybridizes to a DNA molecule comprising the nucleotide sequence of SEQ. ID. No. 157 under stringent conditions~~.

50. (Amended) The expression system according to claim ~~40~~ 49, wherein the heterologous DNA molecule is in sense orientation and correct reading frame.

52. (Amended) A method of producing a recombinant thermostable delta subunit of a DNA polymerase III-type enzyme~~, or subunit thereof,~~ from a ~~thermophilic bacterium~~ *Thermus* species, said method comprising:

transforming a host cell with ~~at least one~~ the heterologous DNA molecule according to claim 1 under conditions suitable for expression of the ~~DNA polymerase III-type enzyme, or~~ delta subunit ~~thereof~~, and

isolating the ~~DNA polymerase III-type enzyme, or~~ delta subunit ~~thereof~~.

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55. (Amended) The method according to claim ~~54~~ 52, wherein the *Thermus* species ~~*thermophilic* bacteria~~ is *Thermus thermophilus*~~, *Aquifex aeolicus*, *Thermotoga maritima*, or *Bacillus stearothermophilus*~~.